Are Some Brain Injury Patients Improving More Than Others?

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Abstract. Predicting the evolution of individuals is a rather new mining task with applications in medicine. Medical researchers are interested in the progress of a disease and in the evolution of individuals subjected to treatment. We investigate the evolution of patients on the basis of medical tests before and during treatment after brain trauma: we want to understand how similar patients *can* become to healthy participants. We face two challenges. First, we have less information on healthy participants than on the patients. Second, the values of the medical tests for patients, even after treatment started, remain well-separated from those of healthy people; this is typical for neurodegenerative diseases, but also for further brain impairments. Our approach encompasses methods for modelling patient evolution and for predicting the health improvement of different patient subpopulations, dealing with the above challenges. We test our approach on a cohort of patients treated after brain trauma and a corresponding cohort of controls.

1 Introduction

Data mining is increasingly used on clinical data for purposes of diagnosis and treatment. In the context of neurodegenerative diseases and of events that disrupt mental functions, like traumatic brain damage and vascular brain lesions, medical researchers want to understand the *evolution* of the patients and to know whether a similar state as for healthy people can be reached. We propose a mining method that captures the evolution of patients subjected to treatment after brain trauma and juxtaposes them to the participants of a control cohort.

The context of our work is the monitoring of patients with a disease or impairment that affects their mental abilities, e.g. Parkinson, brain trauma or coma after excessive alcohol consumption. While there are treatments known to improve patient state, at least for some patients, it is also evident in many cases

that the mental abilities of healthy controls are not recovered. Hence, our task is to identify subpopulations of patients, whose mental abilities become closer to those of some controls. We face two challenges. First, the results of the medical tests on the mental abilities of patients, even after treatment, are still very different from those of the controls, so that a direct comparison between treated patients and healthy cohort participants is not conclusive. Second, we have a lot of clinical data on the patients but much less on the controls, so that the evolution of patients can be modelled but the evolution of the controls cannot. To deal with these challenges, we model the evolution of the patients and identify subpopulations that become (asymptotically) similar to controls.

The study of patient evolution on the basis of timestamped clinical data has been largely influenced by the seminal work of Cox [1] on censored failure times and age-specific failure rates. As pointed out by Fitzmaurice et al., [1] "... was followed by a rich and important body of work that established the conceptual basis for the modern *survival analysis*" [2]. Survival analysis is not applicable to this problem, because there is neither a well-defined target event, nor explicit timepoints to guide the learner. Although there is a control population to juxtapose to the patients, there are no target values to predict, because the assessments of the controls are very different from those of the patients. Hence, we resort to unsupervised approaches to model the evolution of individuals.

The contributions of our EvolutionPredictor are as follows. We model the evolution of subpopulations of patients, on whom only two moments are available, where these two moments are not defined as timestamps[1]. We use this model to compute a future/target state for each patient. We show that the projected target state of patients allows a reasonable comparison to a control population, the recordings of which are very different from the patient recordings.

The paper is organized as follows. In Sec. 2 we discuss related work. In Sec. 3 we present our materials and the mining workflow for modelling evolution and projection of patients after treatment. In Sec. 4, we report on the results of our experiments on brain trauma patients. The last section concludes our study.

2 Related Work

Data mining methods are only recently deployed for analysis of brain pathologies or injury conditions. The authors of [3] analyse data from neuropsychological tests (concerning attention, memory and executive function tests) from 250 subjects before and after a treatment instrumented by a cognitive tele-rehabilitation platform. Their objective is to predict the expected outcome based on the cognitive affectation profile and the performance on the rehabilitation tasks. Our objective is not the prediction of a well-defined outcome, but rather of the future similarity between treated patients and a population of healthy people.

In [4], the authors present an artificial neural network model that predicts in-hospital survival following traumatic brain injury according to 11 clinical inputs.

[1] The one moment is "before" the treatment began, the other moment is "after" the treatment began, but without knowing when exactly the treatment began or ended.

A similar approach was taken by Shi et al [5], who also consider neural networks and logistic regression, but rather study recovery from brain surgery. Andrews et al. discuss methods for prediction of recovery from brain injury, including short-term evolution of patients [6]. The effect of cognitive therapies along longer periods (6 months to 1 year) is studied in [7,8]. Brown et al. learn decision trees on variables that include physical examinations and indices measuring injury severity, as well as gender, age and years of education [7]. Rovlias and Kotsou further consider pathological markers and the output of computer tomography, and learn CART trees [8]. Our study is different from the aforementioned ones, because we do not learn a model on patient recovery (we do not have recovery data), but rather study the evolution of the patients *towards a control population.*

Close to our work are the works [9,10], which predict the progression of glaucoma from cross-sectional (rather than longitudinal) data. The methods learn temporal models on trajectories. A trajectory is built by fitting so-called "partial paths" upon the cross-sectional data: path construction involves selecting one healthy individual and one patient, labelling them as start and end and then re-ordering the remaining cross-sectional instances based on the shortest path from start to end. Our approach shares with [9,10] the need to construct a trajectory of evolution: in principle, we could construct a "partial path" by combining the recordings of the controls and the recordings of the patients during treatment. But this would imply ignoring part of the already avaialble temporal information (pre-treatment data). Moreover, the Trauma Brain Injury dataset of [11], which we use, shows that the control individuals are too different from the patients: this might lead to long and unrealistic partial paths. Thus, we rather build a single projected *moment*, using data before and after the begin of treatment, and do not involve the recordings of the controls in our learning process.

A separate thread of work models and monitors how sub-populations (clusters) evolve over time. The framework MONIC [12] encompasses a set of 'transitions' that a cluster may experience, a set of measures and a cluster comparison mechanism that assesses whether a cluster observed at some timepoint has survived, disappeared, merged or become split at the next timepoint. Later frameworks [13,14] build upon MONIC to explain evolution: they model the clusters and their transitions as nodes, resp. edges of an *evolution* graph. In [15], we build upon [14] to learn a Mixture of Markov chains that capture the evolution of different subpopulations. We take up the idea of subpopulations here, but our goal is to predict rather than model the evolution of the subpopulations.

3 Materials and Methods

Given is a cohort of patients $\mathcal{X}$, for which we measure a set of *assessments* A, e.g. performance at cognitive tests, results of laboratory tests etc, before (t_{pre}) and after (t_{post}) the treatment started. Our goal is to predict *how close* the assessment values of these patients can become to the assessments of a control cohort $\mathcal{Y}$, assuming that the treatment continues. We pursue this goal by first building clusters of patients that evolve similarly from t_{pre} to t_{post}. Then, we

compute a *projection* of each patient's future assessments, using (a) the patient's assessments, and (b) assessments observed in the cluster to which the patient belongs. Finally, we compare these projected assessment values to the values observed in the control cohort. In the following, we first describe the materials of our analysis, then we present the work flow of EvolutionPredictor.

Notation: For each moment t and patient $x \in \mathcal{X}$, x_t is the vector of assessments of x at t: the *instantiation of x at t* or *patient x at t*. The set of moments is $T = \{t_{pre}, t_{post}, t_{proj}\}$, where t_{pre} stands for instantiations before treatment, t_{post} for instantiations after the treatment started and t_{proj} for a future moment, not further specified. Hereafter, we skip the index t, i.e. $x_{t_{pre}} \equiv x_{pre}$.

It is stressed that t_{pre}, t_{post} and t_{proj} are moments ordered in time, but not timepoints in the strict sense, since we do not define a distance among them. The reason is that the duration of treatment among the patients varies, and so does the elapsed time between the incident (traumatic brain injury) and the commence of the treatment. As with many cohorts, the data (cf. subsection 3.1) are too few, so we cannot afford to distinguish among different treatment durations and elapsed time intervals.

3.1 Materials: The TBI Dataset

The **T**raumatic **B**rain **I**njury dataset (TBI) contains assessments on cognitive tests for 15 patients with brain injury and for 14 controls [11]. These tests are recorded once for the controls and twice for the patients – at moments t_{pre} and t_{post}. The cognitive tests are listed on Table 1 (cf. for details [11]).

3.2 The EvolutionPredictor Work Flow

The tasks of our workflow are: (1) bootstrap sampling over the set of patients $\mathcal{X}$; (2) clustering the patient instantiations at each $t \in \{t_{pre}, t_{post}\}$, building a clustering ζ_t; (3) building an evolution graph $G(\zeta_{pre}, \zeta_{post})$ of patients evolving similarly; (4) using the topological space of $G(\zeta_{pre}, \zeta_{post})$ to compute the projection, i.e. the projected instantiation of each $x \in \mathcal{X}$ into the future x_{proj}.

Bootstrap Sampling and Clustering at Each Moment. Our EvolutionPredictor learns from the set of patients $\mathcal{X}$. Since $\mathcal{X}$ is small (as is the case for many cohort datasets), we perform bootstrap aggregation [16] over $\mathcal{X}$. Subsequent instance of each out-of-sample patient (i.e., x_{pre}, x_{post}) are removed. We apply K-Means over the instances at each moment t, and build a set of clusters ζ_t.

Building a Cluster Evolution Graph. We use the concepts of MONIC [12,17] to build a graph of cluster transitions from t_{pre} to t_{post}. For each $c \in \zeta_{pre}$ and $c' \in \zeta_{post}$, we define their intersection as: $c \cap c' = \{x \in \mathcal{X} : x_{pre} \in c \wedge x_{post} \in c'\}$. If $c \cap c' \neq \emptyset$, we draw an edge (c, c') and assign to it the weight $w_{(c,c')} = \frac{|c \cap c'|}{|c \cup c'|}$.

Table 1. Acronyms and description of cognitive tests[2] from the TBI dataset from [11]

Name	Description
TMT-B	Train Making Test-Part B: measures cognitive flexibility (frontal lobe)
BTA	Brief Test of Attention (total score).
WCST-NC	Wisconsin Card Shorting Test: Percentage total score of conceptual level (#categories correctly achieved); also measures cognitive flexibility
WCST-RP	Wisconsin Card Shorting Test: # preservative responses (represent error)
FAS	Phonetic fluency test which uses as cues letters F, A, and S as the initial letters for the patients to start the production of words
ICP	Measures ability to perform daily activities, and awareness of the disease
CIV	Verbal Intelligent Quotient: measures ability to handle verbal material
CIM	Performance IQ: ability to handle visio-spatial/non-verbal material
CV	Verbal comprehension index (VCI)
MT	Working memory (WM): measures the subject's ability to maintain information in short-term memory and recall it
OP	Perceptual organization (PO)
VP	Processing Speed Index (PSI)
IAC	Attention/Concentration Index (ACI)
IMG	General Memory Index (GMI)
IRD	Delayed Recall Index (DRI)

We thus build a directed transition graph $G(\zeta_{pre}, \zeta_{post})$, where the weights of the edges emanating from the same cluster add to 1.0. We define:

$$\mathit{firstmatch}(c) = argmax_{c' \in \zeta_{post}} w(c, c') \tag{1}$$

i.e. the *first match* of a pre-treatment cluster c is the post-treatment cluster with the highest weight among the clusters linked to c.

On Figure 1(a), we show the instantiations of example individuals at time-points t_{pre} (yellow) and t_{post} (aubergine); the corresponding clusters are in (b); the transition arrows and weights are in (c). The yellow star indicates the "projection" of the individual marked as a red star; projections are explained next.

Projecting Patient Assessments into the Future. Let $x \in \mathcal{X}$ be a patient, $c \in \zeta_{pre}$ be the cluster containing x_{pre} ,and c_{fm} be the *firstmatch*(c) (Eq. 1.) Further, we denote the centroid of an arbitrary cluster clu as $\widehat{clu}$. We define the *hard projection* of x from t_{pre} to t_{proj} as the instantiation of x such that the value of each $a \in A$ is determined by the values in x_{pre} and in $\widehat{c}, \widehat{c_{fm}}$:

$$projH(x, t_{pre}, t_{post}) = x_{pre}(a) + (\widehat{c_{fm}}(a) - \widehat{c}(a)) \text{ for each } a \in A \tag{2}$$

[2] The acronyms were derived from the original Spanish names. Therefore, the textual descriptions do not reflect the acronyms. We also provide the English acronyms in parentheses.

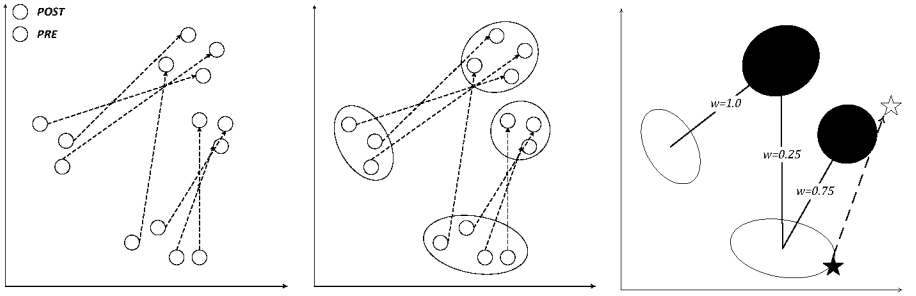

Fig. 1. Clustering, Evolution Graph, Soft Projection: (a) the nodes are patient instantiations at t_{pre} (yellow) and t_{post} (aubergine) – instantiations of the same individual are linked with dashed arrows; (b) clustering is done at each moment and (c) the evolution graph is built by connecting pre- and post-treatment clusters that share individuals; the edge weights are used to compute soft projections, as for the red-star instance

We define the *soft projection* of x from t_{pre} to t_{proj} as an instantiation, the values of which are influenced by all clusters in ζ_{post} that are linked to c:

$$projS(x, t_{pre}, t_{post}) = x_{pre}(a) + \sum_{c' \in \zeta_{post}} \left(\widehat{c'}(a) - \widehat{c}(a)\right) \cdot w_{c,c'} \text{ for each } a \in A \quad (3)$$

where $w_{c,c'}$ is the weight of a transition edge.

Hence, we learn models ζ_{pre} and ζ_{post} on some individuals and then assess the projection location of other (or the same) individuals. On Figure 1(c) we show the *soft projection* of an individual (red star): the projected position is outside both post-treatment clusters, since the individual is located at the rim of the pre-treatment cluster.

4 Experiments

We evaluate our method by first testing whether the projection captures the evolution of the patients reliably. To this purpose, we project from t_{pre} to t_{post}, i.e. on known instances. Then, we show the results of the projection from t_{post} to t_{proj}, which we juxtapose to the controls from TBI dataset. We have no ground truth for this projection, so we rely on the validity of the first projection. We first describe the framework and then discuss our findings.

4.1 EvaluationFramework

To evaluate the performance of the projections we are inspired by the Mean Absolute Scaled Error (MASE) [18], which was originally designed to alleviate the scaling effects of Mean Absolute Error(MAE). To define our variation of

MASE, we assume an arbitrary set of moments $\mathcal{T} = \{t_1, t_2, \ldots, t_n\}$. For an individual x, we define the MASE of the last instantiation x_n as: $MASE(x) = d(x_{proj}, x_n)/\frac{1}{n-1}\sum_{i=2}^{n-1} d(x_i, x_{i-1})$, where $d()$ is the function computing the distance between two consecutive instantiations of the same individual x. This function normalizes the error of EvolutionPredictor at the last moment t_n (nominator) to the error of a naive method (denominator), which predicts that the next instantiation of x will be the same as the previous (truly observed) one. If the average distance between consecutive instantiations is smaller than the distance between the last instantiation and its projection, then MASE is larger than 1. Obviously, smaller values are better.

We further compute the number of times ($Hits()$) the correct cluster is predicted for a patient x. Assume that instantiation x_{pre} belongs to cluster c_{pre} and let c_{proj} denote the *firstmatch*(c_{pre}) (cf. Eq. 1) at the projection moment t_{proj}. We define: $Hits(x) = 1$, if c_{proj} is same as c_{post} (i.e., cluster closest to x_{post}), otherwise $Hits(x) = 0$. Higher values are better.

For model purity, we compute the entropy of a cluster c towards a set of classes ξ, where the entropy is minimal if all members of c belong to the same class, and maximal if the members are equally distributed among the classes. We aggregate this to an entropy value for the whole set of clusters ζ, $entropy(\zeta, \xi)$.

In general, lower entropy values are better. However, the labels used by the EvolutionPredictor are Control and Patient: if a clustering cannot separate well between patient instantiations and controls, this means that the patient instantiations (which are the result of the projection done by our EvolutionPredictor) have become very similar to the controls. Hence, high entropy values are better.

For learning evolutionary prediction model, we use a bootstrap sampling [16] with a sample size of 85% and 10,000 replications. Model validation is done with the help of out-of-sample data. For clustering the union of projected instances and the controls, we use K-Means clustering. We use bootstrap sampling with a sample size of 75% and 1000 replications, and vary $K = 2, \ldots 8$.

4.2 Findings

Validation of the Projection from t_{pre} to t_{post}. In the first experiment, we project the patient instantiations from t_{pre} to t_{post}. Since the true instantiations at t_{post} are known, we use these projections to validate EvolutionPredictor, whereupon evaluation is done with the MASE and Hits measures (cf. subsection 4.1). Figure 2 depicts the hard and soft projections of the pre-treatment patient instantiations, while Table 2 depicts the MASE and Hits values for each patient separately. We perform 10,000 runs and average the values per run.

On Figure 2, we see that the hard projection (yellow) and soft projection (green) behave very similarly. Both predict the patient instantiations at t_{post} very well: the mean values for the projected patient instantiations are almost identical to the true instantiations, and the shaded regions (capturing the variance around the mean) overlap with the variance of the true values almost completely.

The first row of Table 2 enumerates the 15 patients in the TBI dataset, the subsequent rows show the MASE values for the hard, respectively the soft

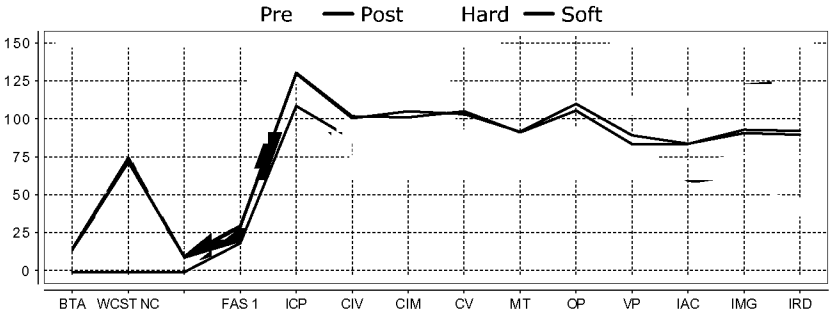

Fig. 2. Variance plots for patient projections, where t_{proj} is set to predict the (already known) instances at t_{post}: the solid lines represent the mean values of the true patient instantiations at moment t_{pre}, t_{post} and of the projected patient instantiations, while the surrounding regions (same color as the solid line) represent the variance of the instantiations; the two projections overlap almost completely with the true distribution at t_{post}, both with respect to the line of the mean and to the region of the variance

Table 2. Hard and soft projection of patients from t_{pre} towards t_{post}, with MASE and Hits per patient: low MASE is better, values larger than 1 are poor; high Hits are better, 1.0 is best; averages over all patients exclude outlier patient #14

IDs	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14	#15	**Avg**
MASE																
Soft	0.29	0.14	0.12	0.19	0.24	0.83	0.13	0.22	0.15	0.21	0.58	0.22	0.37	3.24	0.34	**0.27**
Hard	0.22	0.09	0.10	0.14	0.16	0.90	0.07	0.17	0.13	0.20	0.29	0.23	0.34	3.49	0.42	**0.24**
Hits	0.86	0.62	0.93	0.62	0.95	0.99	0.86	0.89	0.96	0.96	0.54	0.87	0.77	0.81	1.00	**0.83**

projection. The last row shows the Hits value per patient. The last column averages the MASE and Hits values over all but one patients: patient #14 is excluded from the computation, because prior inspection revealed that this patient is an outlier, for whom few assessments are available. All other patients exhibit low MASE values (lower is better), indicating that our projection mechanisms predict well the patient assessments at t_{post}.

Projection from t_{post} to the Future t_{proj}. In the second experiment, our EvolutionPredictor projects the patients after treatment start towards a future moment t_{proj}, which corresponds to an ideal final set of assessments that the patient might ultimately reach through continuation of the treatment. We do not have a ground truth to evaluate the quality of our projections. Rather, we use a juxtaposition of patients and controls, depicted on Figure 3. We show the averages of values per population through a solid line, around which we expand to the variance of values for each variable. The cyan line and surrounding cyan shaded region stands for the moment t_{pre}, denoted as "Pre" in the legend; the

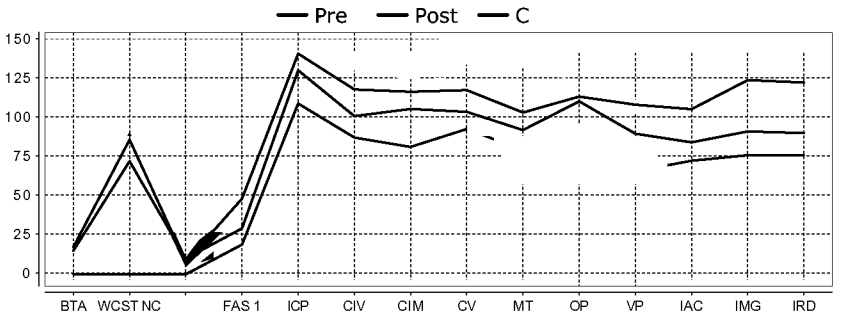

Fig. 3. Average assessment values and variance regions for controls and for patients before (Pre) and after treatment start (Post) for 16 variables: despite some overlaps, lines and regions of patients are mostly distinct from those of the controls

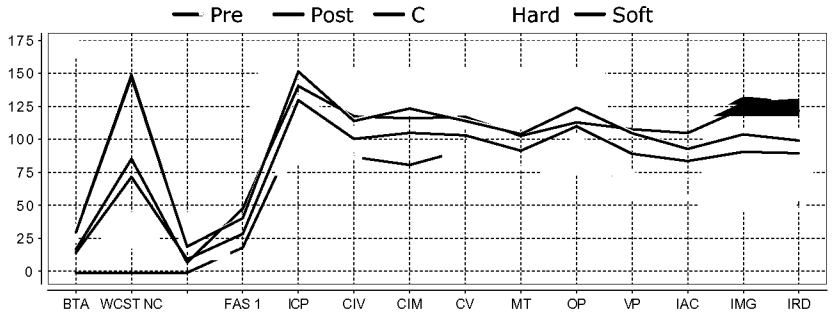

Fig. 4. Average assessment values and variance regions for controls and for patients before (Pre) and after treatment start (Post), and as result of Hard (yellow) and Soft (green) projection: the projected patient assessments are closer to the controls

blue line and region stand for the moment t_{post} ("Post"), while the "Controls" are marked by the red line and red shaded region. Except for Gender and Age, for which controls have been intentionally chosen to be similar to the patients, patients differ from controls. Even where we see overlap between the red area and the cyan (Pre) or the blue (Post) area of the patients, as for assessments CIM and CV, we also see that the average values are different.

Figure 4 shows the same lines and areas for assessments before and after treatment start (Pre:cyan, Post:blue) as the reference Figure 3, but also the projected assessment values (Proj: green/yellow). These projected assessments are closer to the controls, indicating that at least for some of the assessments (FAS1, ICP, CIM, CV, MT, VP), treatment continuation may lead asymptotically to similar values as for the controls.

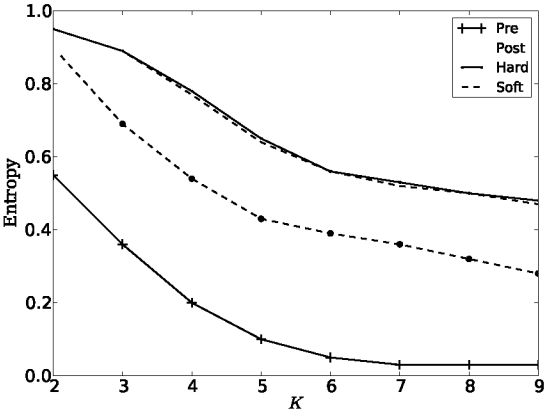

Fig. 5. Controls clustered with the patients before treatment (Pre: red), after treatment start (Post: yellow), with the Hard projection (green) and the Soft one (blue dashed): entropy drops as the number of clusters increases, but has higher (better) values for the projected instantiations, indicating that these are closer to the controls

Clustering Patients with Controls. We investigate whether the patients can be separated from the control population through clustering. We skip the assessments TMT-B, BTA, WCST-NC and WCST-RP, which have been recorded only for some patients. We cluster the controls with the patient instantiations before treatment (Pre: red line), after treatment start (Post: yellow line), with the Hard projected instantiations (green line) and with the Soft projection (blue dashed line). We use bootstrapping with a sample size of 75% with 1000 replications. On Figure 5, we show the entropy, as we vary the number of clusters K. *Higher* values are better, because they mean that the clustering cannot separate controls from patients. High values are achieved only for the projected instantiations.

On Figure 5, the entropy values are very high for the clusters containing controls together with projected patients, whereby soft projection and hard projection behave identically. The high values mean that the clustering algorithm cannot separate between projected patients and controls on similarity; the instances are too similar. This should be contrasted with the clusters containing controls and patients before treatment (red line): entropy is low and drops fast as the number of clusters increases, indicating that patients before treatment are similar to each other and dissimilar to controls. After the treatment starts, the separation between patients and controls on similarity (yellow line) is less easy, but an increase in the number of clusters leads to fair separation. In contrast, projected patients are similar to controls, even when the number of clusters increases: the small clusters contains still both controls and patients.

5 Conclusion

We investigated the problem of predicting the evolution of patients being treated after brain injury and we propose a mining workflow.

Key points: The mining workflow EvolutionPredictor clusters patients on similarity (of their assessments) before and after the treatment began, and then it tracks how each cluster evolves. It builds a cluster evolution graph that captures the transitions of patient clusters before (PRE) to after treatment (POST). Then, our EvolutionPredictor uses the cluster transitions to project each patient to a future moment, on the basis of what is known on the patient's thus far. The core of our approach is the projection mechanism, for which we propose two variants.

We have experimentally validated EvolutionPredictor on the Trauma Brain Injury dataset [11]. We have first applied the method on known data and have shown that the projected values are almost identical to the true ones. Then, we have compared the projected assessments to those of a control population, and we have shown that some patient assessments are projected close to the controls.

We studied treatment after brain trauma, but our EvolutionPredictor is applicable to any impairment, where progression or the process of recovery is of interest. The clusters we find may be of use in personalized medicine.

Shortcomings and Future Work: The projected assessments have not yet be evaluated against the assertions of a human expert about the patients' health state after treatment. We are currently in the process of acquiring such data for an additional evaluation. A further shortcoming is that we ignore the duration of treatment; this is planed as future step.

The evolution of brain trauma or impairment conditions is difficult to measure at the functional level. However, the scholars anticipate that the use of neuroimaging, e.g., MEG, could lead to the detection of progressive changes in the connectivity patterns even *before* they translate into changes at the memory, movement or orientation functions. Regularly recording MEG images before and during treatment of patients, allow a more effective evaluation of treatment by providing hints and indicators about the effectiveness of a particular therapy. A next step for our work will be the integration of MEG data into our mining workflow, to check whether the evolution of patients towards the subcohort of controls can be modelled more effectively with the MEG images.

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References

1. Cox, D.: Regression models and life-tables. Journal of the Royal Statistical Society. Series B (Methodological) 34(2), 187–220 (1972)
2. Fitzmaurice, G.M., Laird, N.M., Ware, J.H.: Applied longitudinal analysis, vol. 998. John Wiley & Sons (2012)

3. Marcano-Cedeño, A., Chausa, P., García, A., Cáceres, C., Tormos, J., Gómez, E.: Data mining applied to the cognitive rehabilitation of patients with acquired brain injury. Journal of Expert Systems with App. 40, 1054–1060 (2013)
4. Rughani, A.I., Dumont, T.M., Lu, Z., Bongard, J., Horgan, M.A., Penar, P.L., Tranmer, B.I.: Use of an artificial neural network to predict head injury outcome: clinical article. Journal of Neurosurgery 113, 585–590 (2010)
5. Shi, H.Y., Hwang, S.L., Lee, K.T., Lin, C.L.: In-hospital mortality after traumatic brain injury surgery: a nationwide population-based comparison of mortality predictors used in artificial neural network and logistic regression models: clinical article. Journal of Neurosurgery 118, 746–752 (2013)
6. Andrews, P.J.D., Sleeman, D.H., Statham, P.F.X., McQuatt, A., Corruble, V., Jones, P.A., Howells, T.P., Macmillan, C.S.A.: Predicting recovery in patients suffering from traumatic brain injury by using admission variables and physiological data: a comparison between decision tree analysis and logistic regression. Journal of Neurosurgery 97, 326–336 (2002)
7. Brown, A., Malec, J., McClelland, R., Diehl, N., Englander, J., Cifu, D.: Clinical elements that predict outcome after traumatic brain injury: a prospective multicenter recursive partitioning (decision-tree) analysis. Journal of Neurotrauma 22, 1040–1051 (2005)
8. Rovlias, A., Kotsou, S.: Classification and regression tree for prediction of outcome after severe head injury using simple clinical and laboratory variables. Journal of Neurotrauma 21, 886–893 (2004)
9. Tucker, A., Garway-Heath, D.: The pseudotemporal bootstrap for predicting glaucoma from cross-sectional visual field data. IEEE Trans. on Inf. Tech. in Biomedicine 14(1), 79–85 (2010)
10. Li, Y., Swift, S., Tucker, A.: Modelling and analysing the dynamics of disease progression from cross-sectional studies. Journal of Biomedical Informatics 46(2), 266–274 (2013)
11. Castellanos, N.P., Paul, N., Ordonez, V.E., Deuynck, O., Bajo, R., Campo, P., Bilbao, A., Ortiz, T., del-Pozo, F., Maestu, F.: Reorganization of functional connectivity as a correlate of cognitive recovery in acquired brain injury. Brain 133, 2365–2381 (2010)
12. Spiliopoulou, M., Ntoutsi, I., Theodoridis, Y., Schult, R.: MONIC – modeling and monitoring cluster transitions. In: Proc. of 12th Int. Conf. on Knowledge Disc. and Data Mining (KDD 2006), pp. 706–711. ACM (August 2006)
13. Ntoutsi, I., Spiliopoulou, M., Theodoridis, Y.: Summarizing cluster evolution in dynamic environments. In: Murgante, B., Gervasi, O., Iglesias, A., Taniar, D., Apduhan, B.O. (eds.) ICCSA 2011, Part II. LNCS, vol. 6783, pp. 562–577. Springer, Heidelberg (2011)
14. Oliveira, M., Gama, J.: A framework to monitor clusters evolution applied to economy and finance problems. Intelligent Data Analysis 16(1), 93–111 (2012)
15. Siddiqui, Z., Oliveira, M., Gama, J., Spiliopoulou, M.: Where are we going? predicting the evolution of individuals. In: Hollmén, J., Klawonn, F., Tucker, A. (eds.) IDA 2012. LNCS, vol. 7619, pp. 357–368. Springer, Heidelberg (2012)
16. Breiman, L.: Bagging predictors. Machine Learning 24(2), 123–140 (1996)
17. Ntoutsi, E., Spiliopoulou, M., Theodoridis, Y.: FINGERPRINT – summarizing cluster evolution in dynamic environments. Int. Journal of Data Warehousing and Mining (IJDWM) 8(3), 27–44 (2012)
18. Hyndman, R.J., Koehler, A.B.: Another look at measures of forecast accuracy. International Journal of Forecasting 22(4), 679–688 (2006)